

# Management of the Pancreas After Pancreaticoduodenectomy

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PANCREATICODUODENECTOMY IS WELL ESTABLISHED in the armamentarium of the surgeon treating peri-ampullary carcinoma. With refinement of operative technique and more enlightened management during the postoperative period, the morbidity and mortality of this procedure have been reduced significantly.<sup>8,15,16</sup> Survival rates in patients with carcinoma of the head of the pancreas, although still less than desirable, are encouraging, and even more gratifying long-term results have been obtained in patients with carcinoma of the ampulla of Vater and distal common bile duct.

In recent years, a variety of methods have been advocated for management of the pancreas after pancreaticoduodenectomy. Pancreatic fistulae and recurrent tumor have stimulated efforts to modify the standard Whipple operation with its accompanying pancreaticojejunostomy.

Four major options are available to the surgeon when pancreaticoduodenectomy is indicated: 1) pancreatic duct-to-jejunal mucosa anastomosis; 2) inversion of the transected end of the pancreas into the jejunal lumen; 3) ligation of the pancreatic duct with oversewing of the transected pancreas; and 4) total pancreatectomy (Fig. 1).

To compare the merits and deficiencies of these modes of management, a retrospective review of the lengthy experience with these procedures at the UCLA Hospital was undertaken and led to the report presented herein.

## Clinical Material

Sixty-five patients underwent pancreaticoduodenectomy at this institution during the 20-year period between 1951 and 1972 (Table 1). Thirty-nine had carcinoma of the head of the pancreas, 16 had carcinoma of the ampulla of Vater, and 10 had carcinoma of the distal

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common bile duct. Their ages ranged from 3 to 84 years; 29 patients were in their seventh or eighth decade of life. The operative mortality for the overall series was 13.8%, but this was reduced to 5.1% during the past 9 years.

Pancreatic fistulae developed in 12 patients, four of whom were among the nine operative deaths. In the other eight patients, morbidity ranged from drainage of pancreatic juice through a small sinus tract for 2 to 4 weeks to intra-abdominal abscesses that required surgical drainage.

## *Pancreatic Duct-to-Jejunal Mucosa Anastomosis*

In ten patients continuity of the gastrointestinal tract was reconstructed by anastomosis of a large dilated pancreatic duct directly to the mucosa of the jejunum. The pancreaticojejunostomy was performed end-to-end in three patients; in seven the transected end of the pancreas was anastomosed to the side of the jejunum. In none of the patients with a dilated pancreatic duct and a direct duct-to-mucosa anastomosis did a pancreatic fistula develop. One of the patients died of superior mesenteric artery thrombosis eight days after operation. A second patient died 9 months postoperatively of recurrent tumor. Four patients died of recurrent tumor at 24 months, 29 months, 33 months, and 35 months. Four patients are still alive, two at 3 years, one at 14 months, and one 3½ months postoperatively.

Five patients with a small pancreatic duct had a duct-to-mucosa anastomosis. Their pancreatic ducts ranged from 2 to 4 mm. in diameter, and the anastomoses varied from four quadrant stitches to several stitches

of fine suture material. Four of the anastomoses were done in an end-to-end fashion, and one was end-to-side. In the patient with the end-to-side anastomosis, a pancreatic fistula developed early in the postoperative course, and he died of hepato-renal failure one month postoperatively. Three patients survived 7½ months, 15 months, and 19 months before death from recurrent disease. One patient is alive at 3 years 9 months.

#### *Invagination of Cut End of Pancreas into Jejunum*

In 38 patients the pancreaticojejunostomy was performed end-to-end in such a way as to invaginate the cut end of the pancreas into the end of the jejunum. The anastomosis was performed between the capsule of the pancreas and the serosal surface of the jejunum with an outer layer of interrupted silk sutures and an inner row of interrupted cat-gut sutures joining the cut edge of the pancreas to the mucosa and sub-mucosa of the jejunum. A small plastic or rubber catheter generally is placed in the duct of Wirsung and either brought down the loop of jejunum and out the abdominal wall or left to lie in the jejunum to be passed spontaneously. The operative reports of 24 of the 38 patients noted such a catheter. A pancreatic fistula developed in eight patients with the invaginating type of anastomosis, seven of whom had a small polyethylene catheter placed into the duct of Wirsung and into the jejunal loop. Two of the eight patients with fistulae died 9 and 13 days postoperatively. Four of the fistulae closed after 2 to 4 weeks of drainage with three of these patients dying of recurrent tumor at 6 months. One fistula drained for 4 months, and the patient underwent four operations for intra-abdominal abscesses before dying at 7 months postoperatively. The most persistent fistula drained for 6 months before closing. The patient died 9 years postoperatively from unrelated causes. Sixteen patients who underwent the end-to-end invaginating anastomosis and did not develop fistulae died of recurrent tumor from 6 months to 120 months postoperatively. Seven patients who had this type of anastomosis without fistula are presently alive at 2½ months, 11 months, 2 years 8 months, 9 years, 10½ years, 13 years, and 15 years postoperatively.

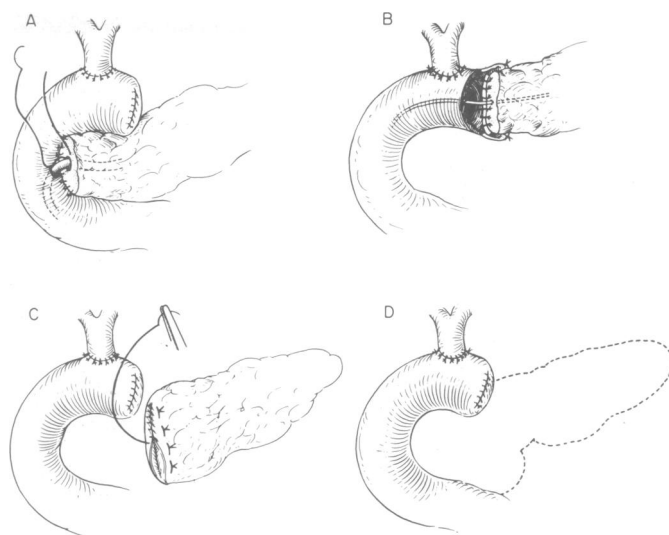


FIG. 1. Diagrammatic representation of four methods employed in the management of the pancreas when pancreaticoduodenectomy is indicated: A) anastomosis of the pancreatic duct to the mucosa of the jejunum; B) inversion of the cut end of the pancreas into the jejunum; C) ligation of the pancreatic duct with oversewing of the transected end of the pancreas; and D) total pancreatectomy.

In five patients found to have a small pancreatic duct, the transected end of the pancreas was buried into an opening made in the side of the jejunum with the bowel wall being sewn down to the pancreas in two layers. There was one pancreatic fistula among these five patients, and in one patient, a bile fistula developed from the end-to-end choledochojejunostomy. One patient died 3 weeks postoperatively of renal failure and sepsis. The other four died of recurrent tumor from 3 to 18 months postoperatively.

#### *Ligation of Pancreatic Duct*

In four patients, the pancreatic duct was ligated and the transected end of the pancreas oversewn with interrupted sutures. Pancreatic fistulae developed in two of these patients, one of whom died 23 days postoperatively. The other fistula closed spontaneously in 3 weeks, and the patient died 9 months postoperatively of recurrent

TABLE 1. *Postoperative Results in 65 Patients undergoing Pancreaticoduodenectomy*

Technique	No. Patients	Operative Deaths	Fistulae	Deaths with Recurrent Tumor	Pancreatic Insufficiency
Duct to mucosa					
Dilated duct	10	1	0	5	2
Normal duct	5	1	1	3	0
Inversion					
End-to-end	38	5	8	20	4
End-to-side	5	1	1	4	1
Ligation	4	1	2	3	—
Total Pancreatectomy	3	0	—	1	—
Total	65	9	12	36	7

tumor. One patient died of recurrent tumor 6 months after operation. The fourth patient lived 7 years 8 months before dying of recurrent tumor.

### Total Pancreatectomy

In three patients the entire pancreas was removed at the time of pancreaticoduodenectomy. It is of interest that marginal ulceration developed in two of these patients at the gastrojejunostomy site during the first two postoperative weeks. One patient died 3 months postoperatively of recurrent tumor, and the other two are alive 8½ and 1½ months postoperatively.

### Discussion

Pancreatic fistula formation, most often the result of breakdown of the pancreaticojejunostomy, with associated erosion, hemorrhage, and infection is the most frequent and serious complication of pancreaticoduodenectomy.<sup>9,10,15</sup> In our series, pancreatic fistulae were associated with four of the nine operative deaths and were the most common cause of postoperative morbidity. In our patients undergoing pancreaticoduodenectomy with partial pancreatectomy, fewer postoperative problems occurred in those who had a direct anastomosis between the pancreatic duct and the mucosa of the jejunum. This was particularly true in the ten patients who had dilated pancreatic ducts secondary to long-term obstruction, none of whom were among those with complications of postoperative fistulae. In addition to a technically easier and better anastomosis with a dilated duct from long-term obstruction, the associated chronic pancreatitis with scarring and fibrosis of the pancreatic capsule renders this anastomosis more secure than one performed in a patient with a normal pancreas. It is of interest that six of these ten patients survived from 2½ to 3 years after operation. The one pancreaticojejunostomy fistula occurring among the patients with a direct duct-to-jejunal mucosa anastomosis was in a patient with a small pancreatic duct sewn with fine suture material to the side of the jejunum.

The end-to-end invaginating type of anastomosis was performed in 58% of our patients undergoing pancreaticoduodenectomy. Eight of the 12 pancreatic fistulae occurred in these patients. The rather tenuous status of suturing to the pancreatic capsule is well recognized. Without an anastomosis of the pancreatic duct to the jejunal mucosa, development of a leak at the anastomotic site is more likely to occur and may be further aggravated by the digestion of pancreatic enzymes. Studies of pancreatic ductal operations have, in general, indicated a superiority of duct-to-mucosa anastomosis when compared to implantation of the transected pancreas in terms of functional results and patency of the pancreatic duct.<sup>1,4</sup>

Brunschwig,<sup>2</sup> Goldsmith *et al.*<sup>6</sup> and Rabwin and Kar-

lin<sup>12</sup> are opponents of pancreaticojejunostomy for several reasons: 1) It is an added and time-consuming step that sets up the potential fistula. 2) When the pancreatic duct is ligated and the stump of the pancreas oversewn, a fistula, should it develop, is less severe and devastating and the pancreatic drainage often clear and less erosive. Pancreatic secretions that leak from a pancreaticojejunostomy appear to be activated by biliary and enteric enzymes and infection with resulting digestion of surrounding tissues. 3) The lack of external pancreatic secretions after ligation of the pancreatic duct or total pancreatectomy can be controlled quite well with oral pancreatic enzymes. 4) When a pancreaticojejunostomy is performed, some question exists as to the continued patency of the pancreatic duct.

Fish *et al.*<sup>5</sup> pointed out that when the duct remains patent, it is rather surprising that pancreatic insufficiency should develop in any patient after pancreaticoduodenectomy since only 10% of the gland is necessary for exocrine function, and most patients retain at least 50% of their gland. In our series, 31 patients survived more than one year postoperatively. Seven of these patients had symptoms and signs of pancreatic insufficiency, twenty-one were normal, and three could not be evaluated. Two of the seven patients with pancreatic insufficiency had a duct-to-mucosa anastomosis, four had an end-to-end invaginating type anastomosis, and one had the transected end of the pancreas buried into the side of the jejunum. The patient in our series who lived 7 years 8 months after ligation of the pancreatic duct was well-controlled on pancreatic enzymes.

We have been impressed by the rather variable nature of pancreatic exocrine replacement required for long-term survivors after pancreaticoduodenectomy. The following case reports illustrate this marked variability.

### Case Reports

**Case 1:** A 46-year-old female was referred to the UCLA Hospital in August 1961, at which time she underwent vagotomy, pyloroplasty, gastrojejunostomy, and gastrostomy for ulcerated diverticulae in the second and third portions of the duodenum. One month later she was reoperated upon for a perforated marginal ulcer at the site of the gastrojejunostomy. She was explored in November 1961 for complete obstruction of the third portion of the duodenum, and pancreaticoduodenectomy was performed for a carcinoma of the head of the pancreas. She did well for five years, but in October 1966 she required still another operation for a marginal ulcer. Further gastric resection and repeat vagotomy were performed; there was no evidence of metastatic disease at this time. Four years later in January 1970, the patient underwent exploratory laparotomy for a rapidly enlarging liver found to be secondary to large tumor nodules. Biopsy revealed suspected islet cell carcinoma metastatic from the head of the pancreas. Subsequent serum gastrin levels were significantly elevated. In July 1970, the patient underwent total gastrectomy. In mobilizing a jejunal limb to reach the esophagus, the blood supply

was injured to the proximal jejunal limb that had been anastomosed to the common bile duct 9 years earlier. When the pancreaticojejunostomy was taken down, complete stenosis of the pancreatic duct was found at the site of anastomosis. There was no route whereby pancreatic exocrine secretion could enter the alimentary tract. Although the patient had never taken pancreatic enzymes, she had not had symptoms of pancreatic exocrine insufficiency.

**Case 2:** A 38-year-old male ex-soldier came to UCLA from Vietnam four months after undergoing a Whipple procedure for a mass in the head of the pancreas discovered during operation for a gangrenous gallbladder secondary to salmonellosis. The pancreatic duct had been ligated and the stump of the pancreas oversewn. Histologic examination of the pancreatic specimen disclosed chronic pancreatitis. Examination at UCLA revealed a left upper quadrant pancreatic fistula. He had not taken pancreatic enzymes at any time since the pancreaticoduodenectomy. He reported having two or three firm, greasy, foul-smelling bowel movements per day. Viokase was begun, and the patient was followed closely. The fistula closed after three months. There was no significant change in the nature or number of bowel movements on the Viokase. Sixteen months later the patient was operated upon for obstructive jaundice found to be due to a small calculus in the common bile duct blocking the choledochojejunostomy. The site of the previous pancreatic fistula was found at the oversewn end of the pancreas. The stump of the pancreas was cut back, the pancreatic duct located, and a pancreaticojejunostomy was performed. The choledochojejunostomy was revised. Postoperatively, pancreatic enzymes were not given. The patient's stool and bile habits were unchanged from their preoperative status. Six months later RATO Test was compatible with pancreatic insufficiency, but the patient was not on medication, had gained weight, felt well, and was working 8 hours per day. His stools and bowel habits were not significantly different than when he was first seen.

Of particular interest is the first patient above who had no pathway whereby pancreatic exocrine secretions could enter the alimentary tract yet had no symptoms of pancreatic insufficiency.

Ligation of the pancreatic duct and oversewing of the transected end of the pancreatic remnant have been utilized to reduce the length of the operative procedure and to eliminate the troublesome pancreaticojejunostomy. In a recent interesting report, Goldsmith and co-workers<sup>6</sup> compared a group of 34 patients who had undergone reimplantation of the pancreatic duct into the gastrointestinal tract with a group of 45 patients who had their pancreatic ducts ligated at the time of pancreaticoduodenectomy. Postoperative morbidity and mortality rates were similar between the two groups. They found that the need for pancreatic endocrine and exocrine supplementation in both groups appeared to be the same, the dosage and length of medication time being variable. At autopsy, patients in both groups showed scarring of the pancreas, stenosis of the proximal portion of the pancreatic duct, and dilatation of the remaining pancreatic duct. Histological sections showed no significant difference between the two groups in terms of exocrine function as reflected in acinar cell structure nor was there

any difference in endocrine function as reflected by the islands of Langerhans. Pancreatic fistulae developed in 27% of their patients who had the pancreatic duct anastomosed and in 22% of those who had undergone ligation of the duct. Although the rate of fistula formation in our four patients was 50% after oversewing of the transected end of the pancreas, use of the procedure would seem to be indicated in carefully selected patients.

In recent years, enthusiasm has been expressed for performance of total pancreaticoduodenectomy in the treatment of some periampullary carcinomas.<sup>7,12,13</sup> The high operative morbidity and mortality associated with total pancreatectomy when it was first advocated by Ross<sup>14</sup> have now been reduced to more acceptable levels. Operative mortality rates for this procedure have been reported to be as low as 9%.<sup>7</sup> Certainly this is within the range of operative mortality reported in most series for partial pancreaticoduodenectomy. Besides removing the often critical pancreaticojejunostomy anastomosis, total pancreatectomy prevents cancer from being left at the line of resection of the pancreas, reduces the incidence of residual tumor in peripancreatic nodes, removes the possibility of new tumor developing from multicentric sites in the remaining pancreas, and prevents implantation and growth of tumor cells present in the ductal system at the time of operation.<sup>3,7,12</sup>

ReMine *et al.*<sup>13</sup> pointed out that chance for cure is not lost when regional lymph nodes are involved with tumor. They suggest that a more thorough job of *en masse* removal of areas of lymphatic drainage can be accomplished when total pancreatectomy is performed.

Collins *et al.*<sup>3</sup> reviewed 11 consecutive Whipple operations performed in their hospital and found that seven patients had lymphatic or nodal invasion of tumor, four had invasion of peripancreatic tissues, five had tumor present at or distal to the line of resection, and one patient had carcinoma *in situ* in areas of the pancreas distal to the primary tumor.

Hicks and Brooks<sup>7</sup> recently reported on 11 patients who underwent total pancreatectomy between 1964 and 1970 and compared them with the 11 patients reported by Collins *et al.*<sup>3</sup> who had partial pancreatectomy in the same hospital between 1956 and 1964. The total pancreatectomy patients had a lower operative mortality rate (9.1% vs. 18.2%), fewer postoperative complications, and a longer average postoperative survival time. Whether the better results obtained in this group were related to the actual procedure or to the fact that the patients were operated upon during the most recent 6 years is speculative.

Pathologic examination of the specimens from the 11 patients who had total pancreatectomy revealed "tumor cells at or distal to the usual Whipple line" in four. It has been documented that the surgeon cannot determine

grossly small areas of remaining tumor at the line of resection.<sup>7,11</sup> Likewise, frozen section specimens cannot exclude remaining small areas of neoplasm. ReMine and co-workers<sup>13</sup> support the idea that the high incidence of "recurrence of tumor" and a large percentage of late deaths after a Whipple procedure probably are secondary to persistence of the primary tumor. Forty-one of our 54 patients who survived the pancreaticoduodenectomy were dead at the time of this report; thirty-six died with recurrent tumor. Autopsy reports were obtained on fourteen, with recurrent carcinoma of the pancreatic remnant being reported in only three patients. This suggests that in our series total pancreatectomy would not have increased significantly the long-term survival rates. Eight of the fourteen patients had liver metastases, and five had obstruction of the choledochojejunostomy by recurrent tumor. Most patients had multiple intra-abdominal metastases involving small bowel serosa, colon, peritoneum, omentum, adrenals, ovaries, or kidneys. One patient had obstruction of the portal vein and inferior vena cava by tumor. Four had pulmonary metastases, and three others had metastases to the pleura without lung involvement.

As noted above, pancreatic exocrine insufficiency does occur in some patients who have had a partial pancreatectomy and gastrointestinal continuity reconstructed by pancreaticojejunostomy. Objections to total pancreatectomy or to ligation of the pancreatic duct on the basis of pancreatic exocrine or endocrine insufficiency are valid but cannot be accepted as reasons for abandoning totally the use of the procedures.<sup>2,9,12,13</sup> In patients with either ligation of the pancreatic duct or total pancreatectomy, pancreatic exocrine function usually may be controlled satisfactorily with one of the commercially available pancreatic extracts (Pancreatin) or whole pancreas preparations (Viokase). We have used Viokase most often because of its more complete hydrolysis of proteins. With dietary and enzymatic regimens, we have been able to control steatorrhea in most of our patients with pancreatic insufficiency.

In patients who have had total pancreatectomy, the pancreatic endocrine function also must be controlled. In general, insulin requirements vary from 15 to 50 units of insulin per day, but the dosage requirements generally stabilize in most patients after a few weeks. Although the diabetes in some patients may be quite brittle, it usually is managed without great difficulty. It is interesting to note that when a patient has been rather stable on a particular insulin dose, an increasing or decreasing need for insulin usually indicates recurrent tumor.<sup>7,12</sup>

Our experience with total pancreatectomy for carcinoma of the head of the pancreas has been limited; nevertheless, we feel that this procedure may have certain advantages in carefully selected patients. For in-

stance, patients with multiple tumor nodules or a mass in the head of the pancreas with marked induration of the pancreas distally in such a way as to prevent localization of the tumor may be candidates for total pancreatectomy. Whether long-term results will justify this extended operation in patients with more localized lesions remains to be seen. Further evaluation would seem indicated.

### Summary

Management of the pancreas at the time of pancreaticoduodenectomy must necessarily vary with each patient. When there is a large dilated pancreatic duct and a good duct-to-mucosa anastomosis can be obtained with the jejunum, this type of reconstruction of the alimentary tract with accompanying choledochojejunostomy and gastrojejunostomy is most desirable. A relatively normally functioning gastrointestinal tract should then be present 3 to 4 months postoperatively. The results of the invaginating type of anastomosis have been less satisfactory with the development of hazardous fistulae and evidence that the cut end of the duct closes in some patients. Our experience with ligation of the pancreatic duct and total pancreatectomy has been limited. Ligation of the duct shortens the operative procedure, and, should a fistula develop, it drains pure pancreatic juice rather than biliary-pancreatic intestinal juices and is less irritating.

Total pancreatectomy may be considered in those patients suspected of having multicentric tumor or patients in whom the changes of chronic pancreatitis cannot be distinguished from neoplastic involvement and the indicated limits of the resection clearly defined.

Control of exocrine function may present a problem regardless of the treatment of the pancreatic remnant, but the degree of deficiency is difficult to predict. Total pancreatectomy adds the concerns of permanent diabetic management to the postoperative care, and although most patients are controlled without undue difficulty, others will require careful prolonged management.

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